

PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
)
Robert J. D'Amato)
)
Serial No.: Not Yet Assigned,)
Continuation of U.S. Patent)
Application Serial No. 09/545,139) **Examiner: J. Goldberg**
)
Filed: **Concurrently Herewith**) **Art Unit: 1614**
)
For: **Methods and Compositions For**)
The Inhibition of Angiogenesis)
With EM-138)

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Box Patent Application
P.O. Box 2327
Arlington, Virginia 22202

Sir:

Prior to examining the present application, please enter the following Preliminary Amendment.

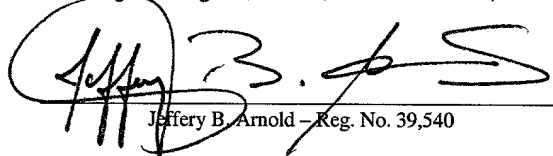
IN THE WRITTEN DESCRIPTION

Please substitute the paragraph beginning at page 1, line 16, and ending at page 1, line 20, with the following paragraph:

=====

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail Label No. EL 910716815 US addressed to: Assistant Commissioner for Patents, Box Patent Application, P.O. Box 2327, Arlington, Virginia, 22202, on December 19, 2001.


Jeffery B. Arnold - Reg. No. 39,540

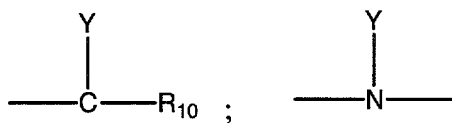
Cross Reference to Related Application

This application is a continuation of U.S. Serial No. 09/545,139, filed on April 7, 2000, which is a divisional application of U.S. Serial No. 08/950,673, filed October 16, 1997, now U.S. Patent No. 6,071,948, which is a continuation application of U.S. Serial No. 08/468,792, filed June 6, 1995, now U.S. Patent No. 5,712,291, which is a continuation application of U.S. Serial No. 08/168,817, filed December 15, 1993, now U.S. Patent No. 5,629,327, which is a continuation-in-part of U.S. Serial No. 08/025,046, filed on March 1, 1993, now abandoned.

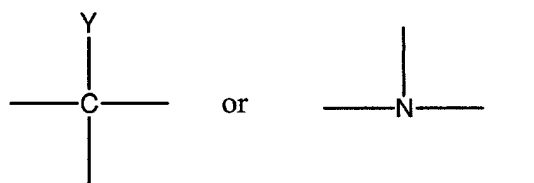
Please substitute the paragraph beginning at page 13, line 1, and ending at page 14, line 5, with the following paragraph:

In the above formulae A), B), and C), R₁, R₂, R₃, and R₄ can be selected from: -H; -OH; =O; straight chained and branched chain alkanes, alkenes, alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; -XO_n or -O-XO_n, (where X=N and n=2; X=S and n=2 or 3; or X=P and n=1-3); and halogens.

In the above formulae A), B), and C), R₅, R₆, and R₇ are each independently selected from:

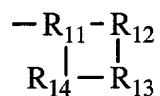


or -O- where Y is optional and is the same as defined above for R₁; and where R₁₀ is the same as defined above for R₁, or (where Y is absent) R₁₀ is =O; and where R₈ is independently selected from:

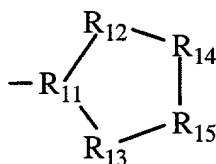


In the above formulae A), B), and C), R₉ is a moiety having formula D), E), F), G) or H):

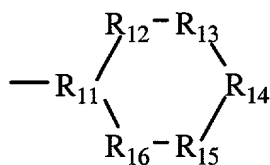
D)



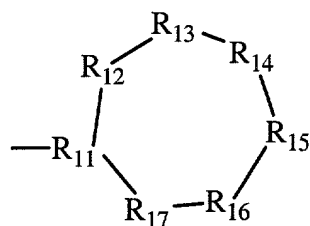
E)



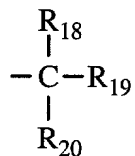
F)



G)

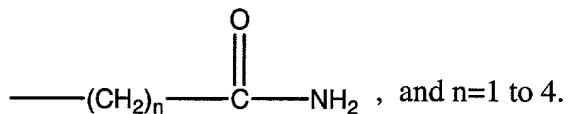
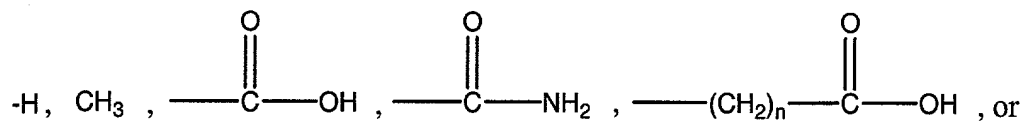


H)



where each of R₁₂-R₁₇ is (independently) the same as defined above for R₅ and where R₁₁ is (independently) the same as defined above for R₈.

In the above formula H), R₁₈, R₁₉ and R₂₀ are independently selected from

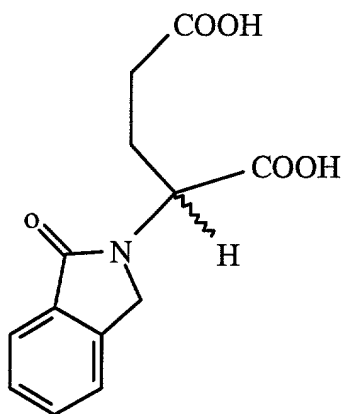


IN THE CLAIMS

Please cancel Claims 1-22.

Please enter new Claims 23-68 as they appear below.

23. (New) A method of treating a neovasucular eye condition associated with angiogenesis in a human or animal comprising administering to said human or animal a pharmaceutically effective amount of EM-138,

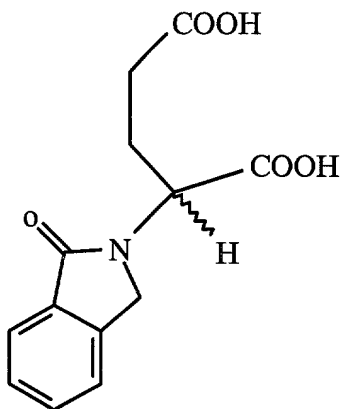


- or a hydrolysis product or a metabolite thereof.
24. (New) The method of Claim 23, wherein the amount administered is between approximately 0.1 and approximately 300 mg/kg/day.
25. (New) The method of Claim 24, wherein the amount administered is between approximately 0.5 and approximately 50 mg/kg/day.
26. (New) The method of Claim 25, wherein the amount administered is between approximately 1 and approximately 10 mg/kg/day.
27. (New) The method of Claim 23, wherein the compound is administered in the form of a tablet or capsule.

28. (New) The method of Claim 23, wherein the compound is administered in the form of a lozenge, a capsule, a cachet, a tablet, a solution, a suspension, an emulsion, a bolus, a powder, a granule, an aerosol, a suppository, a spray, a pastille, an ointment, a cream, a paste, a foam, a gel, a tampon or a pessary.
29. (New) The method of Claim 23, wherein the administration is oral, parenteral, transdermal or topical.
30. (New) The method of Claim 23, wherein the administration is buccal, buccal, rectal, vaginal or nasal.
31. (New) The method of Claim 23, wherein the eye condition is diabetic retinopathy.
32. (New) The method of Claim 23, wherein the eye condition is retinopathy of prematurity.
33. (New) The method of Claim 23, wherein the eye condition is corneal graft rejection.
34. (New) The method of Claim 23, wherein the eye condition is neovascular glaucoma.
35. (New) The method of Claim 23, wherein the eye condition is retrolental fibroplasias.
36. (New) The method of Claim 23, wherein the eye condition is epidemic keratoconjunctivitis.
37. (New) The method of Claim 23, wherein the eye condition is Vitamin A deficiency.
38. (New) The method of Claim 23, wherein the eye condition is contact lens overwear.
39. (New) The method of Claim 23, wherein the eye condition is atopic keratitis.

40. (New) The method of Claim 23, wherein the eye condition is superior limbic keratitis.
41. (New) The method of Claim 23, wherein the eye condition is pterygium keratitis sicca.
42. (New) The method of Claim 23, wherein the eye condition is myopia.
43. (New) The method of Claim 23, wherein the eye condition is Terrien's marginal degeneration.
44. (New) The method of Claim 23, wherein the eye condition is marginal keratolysis.
45. (New) The method of Claim 23, wherein the eye condition is radial keratotomy.
46. (New) The method of Claim 23, wherein the eye condition is macular degeneration.
47. (New) The method of Claim 23, wherein the eye condition is post-laser complications.
48. (New) The method of Claim 23, wherein the eye condition is chronic retinal detachment.
49. (New) The method of Claim 23, wherein the eye condition is optic pits.
50. (New) The method of Claim 23, wherein the eye condition is a hyperviscosity syndrome.
51. (New) The method of Claim 23, wherein the eye condition is chronic uveitis
52. (New) The method of Claim 23, wherein the eye condition is chronic vitritis.
53. (New) The method of Claim 23, wherein the eye condition is ocular neovascular disease.

54. (New) The method of Claim 23, wherein the eye condition is age-related macular degeneration.
55. (New) The method of Claim 23, wherein the eye condition is presumed ocular histoplasmosis.
56. (New) The method of Claim 23, wherein the eye condition is an infection causing retinitis or choroiditis.
57. (New) The method of Claim 23, wherein the eye condition is proliferative vitreoretinopathy.
58. (New) The method of Claim 23, wherein the eye condition is scleritis.
59. (New) The method of Claim 23, wherein the eye condition is Eales' disease.
60. (New) The method of Claim 23, wherein the eye condition is Best's disease.
61. (New) The method of Claim 23, wherein the eye condition is trachoma.
62. (New) A method of treating a neovascular eye condition associated with angiogenesis in a human or animal comprising administering to said human or animal a pharmaceutically effective amount of a composition comprising EM-138,



a hydrolysis product thereof or a metabolite thereof.

63. (New) The method of Claim 62, wherein the effective amount is between approximately 0.1 and approximately 300 mg/kg/day.

64. (New) The method of Claim 62, wherein the effective amount is between approximately 0.5 and approximately 50 mg/kg/day.

65. (New) The method of Claim 62, wherein the effective amount is between approximately 1 and approximately 10 mg/kg/day.

66. (New) The method of Claim 62, wherein the composition is in the form of a tablet, capsule, a lozenge, a cachet, a solution, a suspension, an emulsion, a powder, a granule, an aerosol, a suppository, a spray, a pastille, an ointment, a cream, a paste, a foam, a gel, a tampon, or a pessary.

67. (New) The method of Claim 62, further comprising an additive selected from an anti-oxidant, a buffer, a bacteriostat, a solute which renders the composition isotonic with the blood of the human or the animal, a suspending agent, a thickening agent, a flavoring agent, a gelatin, glycerine, a diluent, or any combination thereof.

68. (New) The composition of Claim 62, further comprising a biodegradable polymer.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amendments in the Specification:

In accordance with 37 C.F.R. 1.121(b), the following replacement pages and lines show all the changes made by the forgoing amendment relative to the previous version of the pages and lines.

Please delete the paragraph beginning at page 1, line 16, and ending at page 1, line 20, and replace it with the following paragraph:

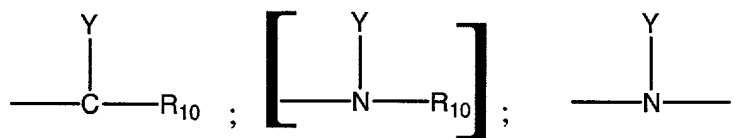
--Cross Reference to Related Application

This application is a continuation of U.S. Serial No. 09/545,139, filed on April 7, 2000, which is a divisional application of U.S. Serial No. 08/950,673, filed October 16, 1997, now U.S. Patent No. 6,071,948, which is a continuation application of U.S. Serial No. 08/468,792, filed June 6, 1995, now U.S. Patent No. 5,712,291, which is a continuation application of U.S. Serial No. 08/168,817, filed December 15, 1993, now U.S. Patent No. 5,629,327, which is a continuation-in-part of U.S. Serial No. 08/025,046, filed on March 1, 1993, now abandoned.--

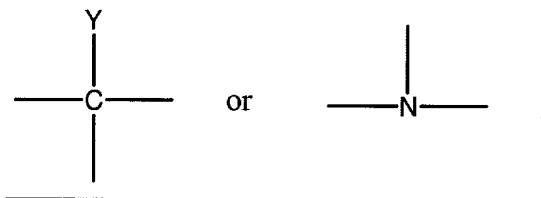
Paragraph beginning at page 13, line 1:

--In the above formulae A), B), and C), R₁, R₂, R₃, and R₄ can be selected from: -H; -OH; =O; straight chained and branched chain alkanes, alkenes, alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; -XO_n or -O-XO_n, [[] (where X=N and n=2; X=S and n=2 or 3; or X=P and n=1-3) []]; and halogens [;] .

In the above formulae A), B), and C), R₅, R₆, and R₇ [, and R₈] are each independently selected from:

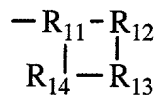


or -O- where Y is optional and is the same as defined above for R₁; and where R₁₀ is the same as defined above for R₁, or (where Y is absent) R₁₀ is =O; and where R₈ is independently selected from:

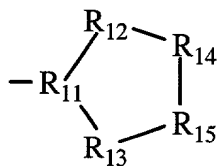


In the above formulae A), B) and C), R₉ is a moiety having formula D), E), F), G) or H):

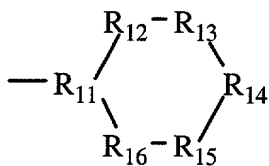
D)



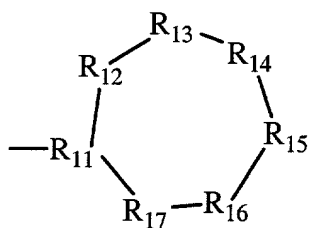
E)



F)

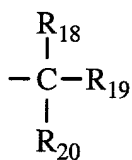


G)



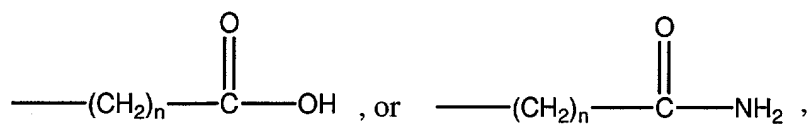
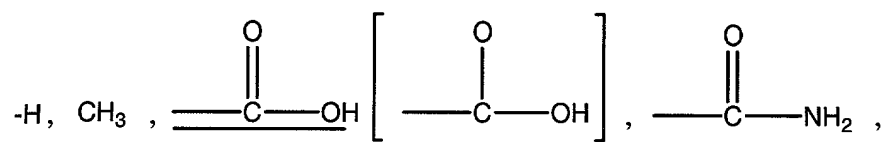
[where each of $R_{11} - R_{17}$ is (independently) the same as defined above for R_5 ;

H)



where R_{12} - R_{17} is (independently) the same as defined above for R_5 and where R_{11} is (independently) the same as defined above for R_8 .

In the above formula H), [where] R_{18} , R_{19} and R_{20} are[,] independently selected from



and n=1 to 4. --

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REMARKS

Status of the Claims

Claims at 1-22 have been canceled. Claims 23-68 have been added to the application. Support for new Claims 23-68 can be found generally throughout the specification.

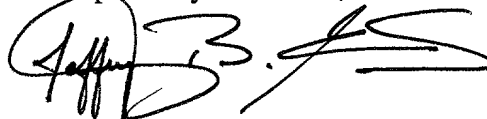
Amendments to the Specification

The amendments to the specification contained herein do not contain new subject matter. Such amendments embody merely the correction of formal matter in the specification without changing the scope thereof. Specifically, the amendments to the specification correct typographical errors in the written description. Support for these amendments can be found in Figures 1-5 and throughout the specification.

CONCLUSION

In view of the above amendments and remarks, Applicant respectfully asserts that all claims are in a condition for allowance and requests that a timely notice of allowance be issued. If issues may be resolved through Examiner's Amendment, or clarified in any manner, a call to the undersigned attorney at (404) 745-2461 is respectfully requested.

Respectfully submitted,



By: Jeffery B. Arnold
Reg. No. 39,540

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Docket No. 05213-0652